(Michel), 0.7 unit. (3) Blood urea, 45 mg. per 100 ml. (4) Serum calcium, 11 mg. per 100 ml. (5) Carbon dioxide combining power, 40 volumes per 100 ml. (6) E.C.G., normal. (7) Blood sugar, 19 mg. per 100 ml. (8) Liver biopsy (immediate): almost complete absence of liver glycogen (0.7%).

Progress in hospital is summarized in the accompanying graph. Adrenaline, 5 minims (0.3 ml.), was given subcutaneously on admission and the blood sugar was estimated after 15 minutes. This showed no real change (18 mg. per 100 ml.). Treatment was then begun with an injection of 40 g. of glucose intravenously, in a 50% solution, followed by a continuous intravenous drip of 9.5% glucose solution. By 4.25 p.m. the blood sugar had risen to 700 mg. per 100 ml. and was associated with a marked glycosuria. No dramatic clinical effect was produced, although the coma appeared to be definitely lighter during the afternoon and evening. The blood sugar had fallen to 84 mg. per 100 ml. by 8.30 p.m., and thereafter remained between 80 and 100 mg. The child continued in a stuporose condition, and during the night he had two generalized tonic-clonic convulsions. Next day a further fit occurred at 5 a.m., following which the child died, the respiration stopping while the heart continued to beat for 15 minutes afterwards.

Post-mortem examination was mainly negative save for lymphoid hyperplasia in the mesentery and ileum, together with fatty change in the liver.

Discussion

The very low blood sugar and almost absent liver glycogen found in this case have also been noted in other examples of vomiting sickness investigated during the acute phase of the illness. Full clinical and pathological details are to be published elsewhere, but results from five cases, including the present one, are summarized in the Table. The rapid

Details of Five Children Admitted with Acute Toxic Hypoglycaemia in the Vomiting Sickness of Jamaica

Case No.	Age in Years	Sex	Mental Condition on Admission	Blood Sugar (on Admission) (mg. per 100 ml.)	Known Length of Coma (Hours) before Treatment	Response to Large Doses I.V. Glucose
1	6	M	Drowsy	6	—	Rapid recovery
2	5	F	Comatose	3	2	Slow recovery (32 hours)
3	8	F	Drowsy—comatose (fluctuant)	5	4	Rapid recovery
4	4	F	Comatose	15	11	Slight improvement. Died
5*	6	M	,,	19	7½	,, ,,

* Present case.

onset, with or without vomiting, of various grades of cerebral depression—varying from drowsiness to stupor to coma—have been observed. Some early mild cases have responded dramatically and immediately to large doses of intravenous glucose, while others have recovered after some hours of treatment.

The present case can be regarded as a fulminant example of so-called vomiting sickness—coma coming on in only one hour, if the father's story is to be believed, while vomiting was virtually absent. Clinical response to a large dose of intravenous glucose was very slight, possibly because of the relatively long period—seven and a half hours—elapsing between the onset of coma and the beginning of treatment. The prognosis in these cases seems directly related to this interval, possibly because irreversible changes can be produced if hypoglycaemia is prolonged.

The toxin responsible for this dramatic clinical syndrome is unknown, but is very probably an accidentally ingested poison, possibly from some wild plant used in one of the "bush teas." The biochemical mechanism producing the hypoglycaemia is also as yet undetermined, but it seems likely that some form of enzyme blockage may be produced, possibly in the enzyme systems responsible for hepatic gluconeogenesis. Whatever this may be, it is temporary and potentially reversible, as if recovery occurs, either spontaneously or following intravenous glucose, it is complete.

While hypoglycaemia is the most striking biochemical finding, there may be other upsets of blood chemistry as yet undiscovered. However, the presence of very low blood sugars in these cases does offer a possible immediate line of therapy, and it seems logical that cases of vomiting sickness should now be treated as medical emergencies with intravenous injections of concentrated glucose solution as soon as possible after the onset of symptoms.

Our thanks are due to Dr. G. Bras for carrying out the necropsy, and to Dr. S. J. Patrick for analysing the liver for glycogen.

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CONGENITAL ABSENCE OF BOTH KIDNEYS

A REPORT OF FOUR CASES

BY

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Agenesis of both kidneys is a rare condition, only 171 cases having been reported since 1663. The four cases occurring at the West Middlesex Hospital described by us bring the total to 175.

The largest number reported was 20 by Potter (1946a, 1946b). These she found in a series of 5,000 necropsies on foetuses and newborn infants, and she estimated the incidence to be 0.3 per 1,000 births. At the West Middlesex Hospital the incidence was four cases amongst 9,940 deliveries (that is, 0.4 per 1,000 births).

The absence of both kidneys is usually accompanied by other gross or multiple deformities (Hinman, 1940). The sex incidence is predominantly male. Bilateral agenesis is compatible with intrauterine life, and does not appear to affect the quantity of liquor amnii. Survival after birth is short; the average duration of life in Potter's cases was 1½ hours. One case is reported to have lived for as long as 21 days, and another for 11 days.

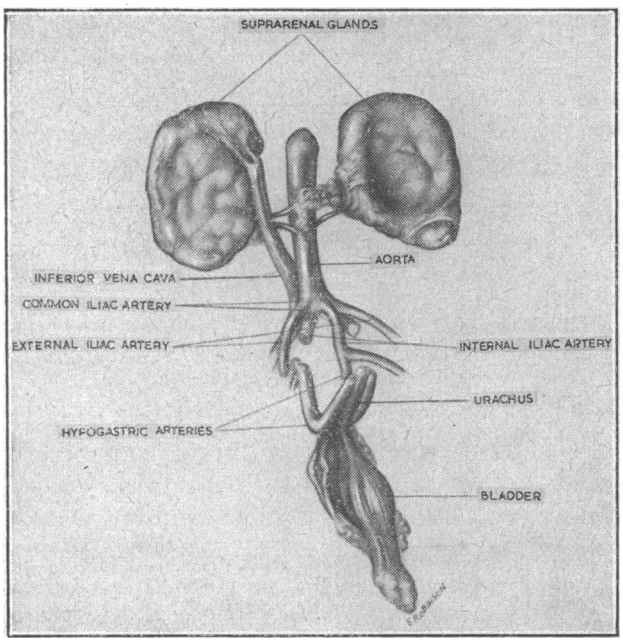
Case 1

The mother, aged 40 years, had four previous normal pregnancies. The last child, aged 6 years, had an undescended right testicle. The other children, one boy and two girls, were normal and healthy. There was no history of congenital deformity in either the mother's or the father's family.

The early antenatal period appeared normal, although the mother later admitted that six weeks after the last menstrual period she had taken about 2.3 g. (35 gr.) of a quinine salt in one day, followed by 85 ml. (3 fl. oz.) of an ergot mixture and two tablets of an unknown substance.

At the 35th week she was admitted to hospital with antepartum haemorrhage due to placenta praevia. The foetus presented by the breech, and the foetal heart was strong and regular. Two weeks later a lower-segment caesarean section became necessary because of severe haemorrhage. The placenta was lying centrally in the lower uterine segment, and it was noted that the liquor amnii was normal in amount.

The child, a boy weighing 2,920 g. (6 lb. 7 oz.), showed a lax skin, generalized cyanosis, and hypotonia. The skull was scaphoid, with a tense anterior fontanelle and an occipito-frontal circumference of 37 cm. (14½ in.). A misshapen left pinna was noted. No abnormality was detected in the cardiovascular, alimentary, or central nervous systems. Rapid grunting respirations, with marked intercostal and subcostal recession and scattered crepitations, persisted throughout life, which lasted 20 hours and 40 minutes.



A dissection from the anterior aspect. The kidneys and renal arteries are absent. Discoid suprarenals are shown.

Necropsy revealed no abnormalities in the brain, thyroid, thymus, heart, spleen, liver, pancreas, and gastro-intestinal tract. A haemorrhagic consolidation was present in the posterior aspects of both lungs, and aeration was present in their anterior margins.

The adrenals were discoid, and measured 4.5 cm. by 3 cm. (see Diagram). There was complete absence of both kidneys, renal arteries, and ureters. A small prostate and bladder were present. Complete descent of the testes had taken place. The penile urethra was patent in the terminal 0.5 cm. A microscopical search for renal tissue failed to reveal its presence.

Cases 2–4

Three other cases of anephrogenesis were discovered in the records of the West Middlesex Hospital. In Tables I, II, and III the details available are summarized and are compared with those of the case described above.

TABLE I.—*Summary of Pregnancies*

Case	Age		Month of Conception	Parity	Abnormality of Pregnancy	Maternal Health	Amount of Liquor
	Mother	Father					
1	40	46	February	4	1. Breech 2. Placenta praevia	Good	Normal
2	18	21	August	0	Mild toxaemia	Good	No record
3	45	?	September ?	5	None	Mitral and pulmonary systolic murmurs	Very little
4	25	52	February	0	Mild toxaemia	Diffuse enlargement of thyroid for many years	No record

TABLE II.—*Summary of the Infant Data Prior to Death*

Case	Duration of Pregnancy in Weeks	Birth Weight	Sex	Weight of Placenta	Duration of Life
1	36	6 lb. 7 oz. (2,920 g.)	M	1 lb. 3 oz. (548 g.)	20 hr. 40 min.
2	34	3 lb. 13 oz. (1,730 g.)	F	12½ oz. (354 g.)	2 hr. 20 min.
3	34	4 lb. 14 oz. (2,210 g.)	M	No record	28 hr. 30 min.
4	40	5 lb. 12 oz. (2,608 g.)	M	9 oz. (255 g.)	Stillborn

Aetiology

The present knowledge of the aetiology of congenital abnormalities is reviewed fully by Warkany (1947) and Fraser and Fainstat (1951). The two main groups are: (1) genetic and (2) environmental. The latter includes nutritional deficiencies and chemical, physical, endocrine, infectious, and mechanical agents. The timing of the environmental disturbance has been shown experimentally by Ingalls *et al.* (1950) to be important in deciding the site and nature of a congenital defect. These factors are applicable to congenital deformities of the renal tract.

Arey's (1946) calendar of human development shows that by the fourth week of embryonic life the pronephros has

TABLE III.—*Clinical and Pathological Findings*

Case:	1	2	3	4
Head	Scaphoid skull; misshapen left ear	Asymmetrical	Considerable head moulding; bilateral accessory auditory auricles	Dolichocephaly; cranial bones friable and thickened
Respiratory system	Cyanosis; congenital atelectasis	Cyanosis; congenital atelectasis	Cyanosis; congenital atelectasis	Bilateral pulmonary hypoplasia
Cardiovascular system	No abnormality	No abnormality	No abnormality	Patent interventricular septum
Alimentary system	No abnormality	No abnormality	Intestinal adhesions; ectopic caecum	"Hour-glass" constriction of stomach
Locomotor system	No abnormality	Limited flexion and abduction of both hips; hypermobility of right knee	No abnormality	Deformed hands and feet; limbs splinted against trunk
Urogenital system	Absence of both kidneys and ureters; rudimentary bladder	Absence of both kidneys and ureters; failure of fusion of Müllerian ducts; bladder elongated	Absence of both kidneys and ureters; small bladder	Absence of both kidneys and ureters; bladder present

reached maturity and begun to degenerate. Between the fourth and sixth weeks the mesonephros, mesonephric duct, ureteric bud, and metanephros are undergoing active developments. The future of the kidney depends upon: (1) the successful caudal migration of the mesonephric duct; (2) the sprouting of the ureteric bud; (3) the formation of the metanephros; and (4) a combination of these three processes. The "critical period" of renal formation is between the fourth and sixth weeks of intrauterine life, and it is during this period that one would expect noxious environmental influences to be most effective.

Discussion

It is suggested that Case 1 is an example of congenital abnormality caused by disturbed environment. Six weeks after her last menstrual period, in a regular cycle of 6/27, the mother swallowed 2.3 g. (35 gr.) of a quinine salt within 24 hours, and later 85 ml. (3 fl. oz.) of an ergot mixture and two tablets of an unknown substance. The probable age of the embryo at this time—4 to 6 weeks—covered the important developmental periods of the mesonephric duet, cloaca and ureteric bud.

Quinine salts are known to be protoplasmic poisons with a specific nephrotoxic action. They are readily absorbed into the blood stream, and Dilling and Gemmell (1929) showed that quinine crosses the placental barrier at term. Huggett and Hammond (1952) state that placental permeability of different agents varies according to the stage of development. We have been unable to trace experimental proof that quinine reaches the human ovum from the maternal blood in the first few weeks of pregnancy. However, we submit that it is not unreasonable to regard quinine as the agent responsible for the agenesis of the kidneys in Case 1. Our assumption is that the drug acted direct on the rapidly differentiating renal tissue.

The deformity of the left pinna is interesting. Potter noted certain facial characteristics, which included large low-lying ears with cartilaginous dysplasia. In a six-weeks embryo the external ear is beginning development around the first branchial cleft. Therefore it may be supposed that disordered differentiation of the tissues at this time was the result of an insult, the timing of which coincided with the quinine administration.

One weakness in our hypothesis is the fact that quinine and other drugs are often taken as abortifacient measures during the early weeks of pregnancy and yet bilateral anephrogenesis is rare. There are three points to make in reply. First, the drug must be taken at the correct time in the development of the renal tract; the margin of error in time allowance is probably very small. Secondly, it is necessary to assess the incidence of anephrogenesis in the embryos and foetuses of abortions. Thirdly, the dosage and concentration of the drug must be sufficiently great.

Summary

Four cases of congenital absence of both kidneys are reported. One of these cases is described in detail.

The aetiology of the condition is discussed. The fourth to sixth weeks of embryonic life are the "critical period" during which development of the kidneys is taking place, and is the time when noxious environmental factors could exert their most damaging effects.

Quinine, taken by the mother of one case in a large dose six weeks after her last menstrual period, is suggested as a possible cause of the renal agenesis.

We wish to thank Dr. M. Dynski-Klein, Mr. D. M. Stern, and Miss I. M. Titcomb for allowing us to report these cases under their care and for access to their records; Dr. A. C. Counsell for his careful pathological examinations; and Miss S. Robinson for the drawing.

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USE OF UNSATURATED FATTY ACIDS IN THE ECZEMAS OF CHILDHOOD

BY

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Burr and Burr (1929, 1930) and Burr *et al.* (1932) showed that the total exclusion of fats from the diet of young rats produced a deficiency disease with caudal necrosis, red and somewhat swollen feet, and scaliness in the hair of the back. At the same time the growth of the animals was arrested and there was much loss of weight. This condition was not improved by adding non-saponifiable fats to the diet, but was cured by the unsaturated fatty acids (U.F.A.s), particularly linoleic and linolenic acids.

This work stimulated Hansen (1933), who first made the suggestion that U.F.A.s might be useful in treating infantile eczema. He demonstrated that there was a diminution of these acids in the serum of eczematous children, and he claimed that the addition of U.F.A.s to their diet caused a clinical improvement which was associated with a rise in the iodine number, an index of the non-saturated fatty acids in the serum. Shortly afterwards Cornbleet (1935) reported good results in a series of 85 cases of eczema which had been treated with fresh lard by mouth, but there seems to be no reference to any control in his investigation. Taub and Zakon (1935) found no benefit in eight cases of atopic eczema (Besnier's prurigo, disseminated neurodermatitis) which they treated with linseed oil by mouth, and also pointed out that the use of linseed or cotton-seed oil might be dangerous, as the patient could be sensitive to these sources of U.F.A.s. Ginsberg and Bernstein (1937) found satisfactory improvement in three adults in a group of 11 with atopic dermatitis and in four out of six children. They also pointed out, however, that two children receiving the same local treatment and no added U.F.A.s improved in the same time. Finnerud, Kesler, and Weise (1941), using fresh lard in older children and adults, had a satisfactory response in about half their cases. Hansen, Knott, *et al.* (1947) reported on the study of 225 cases of eczema, of whom 123 were under the age of 2 years, 67 were from 2 to 15, and 35 were 16 and over. During these trials they used many forms of local treatment, including boric acid, zinc paste, sulphur, resorcinol, and occasionally coal-tar. Their results were poor in only 37 of the 148 cases treated with supplementary fatty acids, while 18 of the 48 controls were unsatisfactory in the same